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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex Parte JAY GOLDSTEIN, MICHAEL ROTHMAN,
and WHE-YONG LO

Appeal 2010-006562
Application 10/691,928
Technology Center 1600

Oral Hearing Held: October 18, 2011

Before TONI R. SCHEINER, LORA M. GREEN, and STEPHEN WALSH, *Administrative Patent Judges*.

APPEARANCES:

ON BEHALF OF THE APPELLANTS:

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The above-entitled matter came on for hearing on Tuesday, October 18, 2011, commencing at 9:05 a.m., at the U.S. Patent and

Trademark Office, 600 Dulany Street, Alexandria, Virginia, before Timothy J. Atkinson, Jr., a Notary Public.

THE USHER: Good morning. Calendar No. 17, Appeal No. 2010-006562, Mr. Terapane.

JUDGE SCHEINER: Thank you. Good morning.

MR. TERAPANE: Good morning. How are you?

JUDGE SCHEINER: I'm fine, thanks. I just wanted to let you know that Judge Walsh is joining us from an undisclosed location.

MR. TERAPANE: Location unknown? Okay, good morning.

JUDGE WALSH: Good morning.

JUDGE SCHEINER: Judge Walsh, we're going to start, whenever you're ready.

MR. TERAPANE: Okay, thank you. My name is Michael Terapane; I'm appearing on behalf of the applicants in this case, and with me today is Dr. Jay Goldstein --

JUDGE SCHEINER: Good morning.

DR. GOLDSTEIN: Good morning.

MR. TERAPANE: -- who's an inventor on the application, and he's going to speak briefly at the end.

JUDGE SCHEINER: May I just make sure that, Steve -- Judge Walsh, can you hear us all right?

No. Can you hear what's going on in the hearing room? No.

JUDGE WALSH: Yes.

JUDGE SCHEINER: Yes.

MR. TERAPANE: Yes.

JUDGE SCHEINER: Okay.

MR. TERAPANE: Okay.

JUDGE SCHEINER: Can you hear Mr. Terapane?

JUDGE WALSH: Yes.

JUDGE SCHEINER: Okay.

MR. TERAPANE: Okay.

JUDGE SCHEINER: All right, now I'm probably going to -- I'm supposed to push this button when I speak to you and turn it off when I don't, so I think I'll probably mess that up a couple times because I'm not used to it.

MR. TERAPANE: We'll work through it.

JUDGE SCHEINER: All right, signing off, okay.

MR. TERAPANE: Okay, thank you. So I think we'll just jump in with the -- with the rejections that were set forth by the Examiner. I'll address them in the order that they were presented.

The invention here is the discovery that you could combine with an antifungal agent a low to low-medium potency steroid and have that effectively treat topical fungal infections while avoiding side effects that have been associated with high-potency formulations like Lotrisone, which was the standard at the time.

So the first reference that was cited by the Examiner was the '056 patent to Quigley, and the first thing I want to point out in Quigley is, there is a table at columns 4 and 5 which provides a list of various formulations of different steroids. And something I want to point out in this table is, and it's very important to keep this in mind, is that there are really at least, and really three critical factors that determine potency of a steroid. The first is, obviously, the drug itself. The second is the concentration, which is another

sort of obvious factor, but the third one is the way in which it's formulated, and so creams are different than lotions, which are different than ointments.

And I think more to the point is, different creams can have different potencies. So if you look in that table, for instance, there are three different creams for betamethasone that actually are classified as I, II and III. So there's lots of variability here in terms of what the potency ends up being, based on how it's formulated, what the drug is, and what the concentration is.

Now really, the specific rejection that the Examiner raised here, he went right to Table G, which is in column 11, which is really a prophetic example, it's sort of a representative prophetic example of how you can make a lotion within the scope of this patent. It has general disclosure with respect to the concentration range of the steroid; doesn't necessarily reference a specific steroid that you would use.

The Examiner took that table, took .02 percent and said, well, if you combine those things, you end up getting a .02 percent lotion, which is in the table that I just referred to, classified as a low or medium potency steroid. So there's a couple of issues with this.

The first off, is the disclosure in this reference is incredibly broad. There's no disclosure here to specifically select a low or low-medium potency steroid. So under the standard articulated by *In re Arkley*, by the Court, where it said, you know, if it's so broad that you'd have to selectively pick and choose to be able to get to something, that's not anticipatory. And that's really what we have here, and the Examiner was forced to sort of pick and choose from various parts of this to try to come up with something that he thought anticipates the claims.

Not only in addition to that, but we don't even know that this lotion formulation that's prophetically described here is, in fact, the same lotion that's listed in the table. And as I just mentioned, because even the same vehicles can have different potencies, so one cream could be more potent than another cream or vice versa, we don't even know that the lotions would have the same potency.

The Examiner also failed to recognize, I think, or at least to consider, the working examples that follow these prophetic examples. So if you go to, for example, example 10, which is actually a formulation that was prepared within the patent, this is a lotion formulation. But notice that the potency of betamethasone, which is the steroid that he focused on because it's described as the preferred one in the patent, the concentration here is three times the concentration of that low-potency lotion formulation that's described in the table. And so this is going to be a much, much higher-potency formulation than what the Examiner alleges is disclosed here.

And then finally, I just want to add, when you get past those working formulation examples that were made and we actually get into some examples that are comparing efficacy, and this is examples 12 and 13, what they ultimately chose were creams that are high-potency formulations. And so there's just -- there is no disclosure in this reference, either explicitly or inherently, to choose a low to low-medium strength steroid formulation in order to effectively treat fungal infection while avoiding side effects.

JUDGE WALSH: Mr. Terapane, I have one question about the formulations that you just went through.

MR. TERAPANE: Sure.

JUDGE WALSH: Earlier in the Quigley patent, the Examiner had directed attention to column 1 at around lines 28 to 32 or so.

MR. TERAPANE: Yes.

JUDGE WALSH: And it seems there that Quigley addresses at least what seems to be a very similar problem as to one your inventors are addressing. And then in column 2, at about line 25, Quigley says that and then it shows their formulation delivers the antifungal agent and the steroid, but it minimizes penetration of skin and avoids side effects. So what weight should we give that part of the disclosure?

MR. TERAPANE: So, I think there's two things to keep in mind in view of that disclosure. The first is I think it's telling that there's actually no data in the patent with respect to side effects. There is data with respect to efficacy in treating fungal infection, but we actually don't know that the formulations they made and ultimately studied avoided side effects. I mean, there's no data that, well, they did an irritation study or some other sort of study to say that.

Secondly, we don't know in what context that statement is made with respect to potency of the steroid formulation. In other words, if you look at what was done ultimately in terms of the working examples that were done, and really even in terms of most of the prophetic examples, the formulations are all either mid-potency at a minimum, but more likely high-medium or high-potency steroids. So I don't think there's a disclosure here, either explicitly or inherently, of a low to low-medium steroid formulation which effectively treats the fungal infection while avoiding side effects.

Remember, there's two things here: You got to avoid side effects, but you also have to effectively treat the underlying fungal infection, or what's

the point? So I think these are general statements but they're not tied to anything in particular in terms of potency of the steroid, but more to the point, there's no data that, in fact, shows that they were able to even accomplish avoiding side effects with respect to the working examples that they have, which is really all we have to go on in terms of the potency of the steroid that they're using.

The prophetic formulations are so broad that you literally would have to pick and choose to get to even a low to low-medium like, which is what we are claiming, and there's no evidence, in fact, that that was effective for what they were looking at. So I would even argue I'm not sure they're --

JUDGE WALSH: Assuming --

MR. TERAPANE: I'm sorry, go ahead.

JUDGE WALSH: Assuming for the moment that we take your point about picking and choosing, do you want to also address at this time the portion of the quick disclosure that the Examiner referred us to at column 5? And that was about line 55 or so. I mean, if you want to save this for -- discussion, that's fine too, but it seems to be related to what you were saying.

MR. TERAPANE: No, I think we can address that here as well. I mean, yeah, there's a general statement here that says if the potency is high you can use a little bit less; if it's low, you can use a little bit more. I'm not sure that's really a teaching of selecting a low to low-medium potency steroid. I think what it's saying is is that if you started with a low, you would increase the concentration, you'd increase the amount, which ultimately means you would increase the potency.

And so I think if you look at that in the context of what's taught in the prophetic and working examples, what you end up with is a formulation which is, at the weakest, a mid strength, but more likely is actually a medium-high to high potency formulation, and that's what they're looking at.

And I think that's supported by the fact that if you look in the examples too, their treatment times are fairly short. I mean, they claim that they get basically 70 to 80 percent efficacy after 8 days. I mean, that's a fairly short treatment period, so I think they're focused on, you know, basically, a means of using a medium to medium-high or high potency formulation, but being able to shorten duration of treatment time so that you avoid side effects that might be associated with it.

There's no teaching because nobody recognized at the time that a low to low-medium steroid formulation would, in fact, not only avoid side effects; you might have guessed that that certainly may have been the case, but you wouldn't have guessed it would have effectively treated the underlying fungal infection as well.

And that does -- you're right, that does tie into the obvious, and matter of fact, I can probably go over that relatively quickly when I get there, because a lot of the same arguments will apply. Okay.

The second reference that was cited for anticipation was the Burnett reference, and a couple of general -- well, not general, specific comments here about this. The first thing to keep in mind is that Burnett teaches anhydrous compositions, that is, those without water or very little water. In sort of the terms of the art, that typically means an ointment; ointments are typically topical formulations that don't contain water.

One of the things you will notice if you look in that table back in Quigley that had some representative formulations and their potencies, ointments are much, much higher potency than, say, formulations that contain water, like creams or lotions. So clearly, the focus here is going to be on a formulation that likely is at least medium if not medium-to-high potency formulation by virtue of the fact that it's an ointment.

On top of that, it also includes a penetration enhancer which is going to enhance penetration of the steroid into the skin. Matter of fact, they actually talk about the fact that what they want to do here is, they want to drive it into the dermis and the epidermis. They're trying to avoid getting the steroid to a particular receptor to avoid systemic side effects, but in fact what they're really trying to do is get it into the skin which is going to actually increase the chances that you're going to have these adverse local side effects that we, actually, specifically avoid in the claim language that we have.

And so the Examiner here, I think, once again pointed to a specific formulation of Desonide at a certain percent and said, you know, this is termed to be a low or medium-strength formulation. However, because these are anhydrous formulations which are always going to be higher potency, so you're already looking at a medium to medium-high to begin with, and on top of that you now have a penetration enhancer which is going to increase penetration of the steroid into the dermis and the epidermis, you're more likely to get side effects, the local side effects that we're trying to avoid.

JUDGE SCHEINER: Is there anything of record that supports your statement that the anhydrous formulations are typically, or–

MR.TERAPANE: Sure. Actually, if you look in the Quigley, that table in Quigley–

JUDGE SCHEINER: Okay. I mean, oh, okay, but have you discussed that on the record?

MR. TERAPANE: I know we have, we do have some discussion in the Appeal Brief and in the Reply Brief about the fact that the potency differs based on the formulation, the vehicle carrier.

JUDGE SCHEINER: Okay.

MR. TERAPANE: I don't know if that specific point was made, but we certainly talked about the fact that when you go from lotion to cream to ointment, those potencies are going to differ because of the carrier vehicle.

JUDGE WALSH: Okay.

MR. TERAPANE: And like I said, even within the same carrier vehicle, within various creams or lotions or ointments, you're going to get different potencies as well.

So with respect to Burnett, I really think that's the main point that we want to make here, is that you have an ointment which is anhydrous, which is going to increase potency, in combination with a penetration enhancer which is going to increase potency because it increases absorption of the steroid into the dermis and the epidermis. And, therefore, you're more likely to get the local side effects that we're trying to avoid. And once again, no explicit teaching here of using a low or low-to-medium strength potency steroid formulation to treat a fungal infection like we're claiming.

Any questions on Burnett?

JUDGE SCHEINER: No.

MR. TERAPANE: Okay. Then the Examiner made an obviousness rejection over Quigley by itself. I'm not sure I need to add much more.

JUDGE SCHEINER: No.

MR. TERAPANE: And I addressed, I think, the question you had raised with respect to obviousness in that certain passage. So, certainly, the arguments we made previously apply here. Once again, we think the focus here is really on, at best medium, but more likely a medium-high to high-potency formulation based on not only the prophetic examples but the working examples.

The second obviousness rejection was with respect to Burnett in combination with Shah. We've talked about Burnett and the issues that we think are there. The Examiner cited Shah for a specific purpose which is -- I think, according to him, he cited it because he wanted it to provide some other antifungal compounds that weren't explicitly disclosed in the Burnett reference. However, he sort of ignored the rest of the disclosure.

First of all, Shah is also a composition containing a penetration enhancer, so you're going to be increasing, once again, absorption of the steroid and, therefore, increasing the potency. But also, Shah specifically teaches at columns, excuse me, at the top of column 4 -- this is starting at line 3 -- that mid-potency steroids are preferred in that reference, because there are problems with either strong or -- and low-potency steroids. So if you were going to combine these two references, and you have to consider the references as a whole, which the Examiner did not do here -- if I'm combining Shah with Burnett, what I'm doing is I'm making a formulation that contains a mid-potency steroid with a penetration enhancer, which means I'm going to end up increasing the potency, ultimately, of it to maybe

medium-high, based on the fact that it's going to be absorbed deeper into the skin. But once again, there's nothing here to support choosing a low to low-medium potency steroid as a means for effectively treating a fungal infection while avoiding, you know, the local side effects that we're trying to avoid.

JUDGE WALSH: Mr. Terapane, you said that the -- had two comments on your arguments about the first. The Examiner pointed out that Burnett and your claims both -- and second, the Examiner argues over a claim interpretation of Claim 1, at the wherein clause. The Claim reads "The composition does not put -- had caused undesirable local side effects." The Examiner took the opinion that one could have a composition with steroids to penetrate the skin, but they don't cause undesirable side effects, and that that would be -- would you comment on those two points?

MR. TERAPANE: Sure. So I think with the first, with respect to the propylene glycol comment that he made, there's a very telling passage, and this is in Shah once again, at the bottom of column 2, starting at line 65, which says "It is well known that the effectiveness of a penetration enhancer depends on the type of drug molecule and the composition of the formulation."

So what that means is, just because we may say that propylene glycol could be a solvent in a particular formulation, doesn't mean it acts as a penetration enhancer, because the effectiveness of something to be a penetration enhancer depends on the drug that you are formulating, but also what other components are in that formulation. Matter of fact, Shah says specifically, you can see serious drop-off in the effectiveness of enhancing penetration as you start adding multiple components to the composition.

So I think that's -- it's a bit of a red herring in the sense that he really took it out of isolation and said, okay, if you've got PG and they've got PG, it's got to be the same thing. That's not it at all. You've got to look at the specific formulation, what else is there, what the drug is, and whether or not what you're using actually acts as a penetration enhancer. Not to mention most of the time, PG is also used in combination with other materials to enhance penetration. So that would be my counter with respect to that.

With respect to his interpretation of the Claim, I'm not sure that I exactly followed the point that he was trying to make. I mean, I think when you have a topical fungal infection, it's going to be located primarily on the skin, it's going to be somewhat into the skin, and so no matter what formulation you apply, you're going to get some absorption into the skin.

What we're trying -- you know, what we're claiming and what this composition is designed to do is to minimize that absorption into the skin so that you don't get those local side effects that you see with the high-potency formulations. And so I think, you know, to distinguish us from the prior art, I mean the prior art really said, we are trying to get this into the skin, that's what we're trying to do; we want it deep into the dermis and the epidermis.

Well, that's fine. I mean it gets you in contact with the fungal infection. However, because you are starting with a, excuse me, with a mid-potency steroid, or even a high potency steroid, you now have this very strong active agent in the skin which then gives rise to these local side effects, which is, as Dr. Goldstein's going to attest to, are in some ways worse than the actual underlying fungal infection in terms of the symptoms that the patient is suffering from.

And so I'm not sure I understand the point he's trying to make, but I think we've clearly distinguished that the references that have been cited versus what we're claiming.

JUDGE WALSH: Thank you.

MR. TERAPANE: Okay. How much time do we have?

JUDGE SCHEINER: Just a few minutes.

MR. TERAPANE: Okay. He only needs maybe, probably, three to five minutes tops --

JUDGE WALSH: Okay, Dr. Goldstein.

MR. TERAPANE: So, okay. Thanks.

DR. GOLDSTEIN: Good morning, Your Honors.

JUDGE SCHEINER: Good morning.

DR. GOLDSTEIN: My name's Jay Goldstein; I'm a dermatologist, I've been in practice for 30 years. Tinea, or a fungus, or ringworm is one of the more common things we see in practice. It presents usually as red, scaly areas on the skin, often associated with a lot of itching, and so severe it can keep patients up at night.

At the time of our filing in 2002 or so, the way of treating fungal infections was twofold: one is by the use of an antifungal alone; and the second was with the use of an antifungal with a high-potency topical steroid. This was known as Lotrisone; it was a combination of betamethasone dipropionate, which is a high-potency class I or II steroid in association with an antifungal.

The problem with treating only with an antifungal is that it doesn't alleviate the itching or pruritus in the patient until the fungal infection clears, which can be in the neighborhood of four to six weeks, if not longer. So

although you're, effectively, treating the fungus; the symptoms continue, the patient is still miserable, there's still scratching. So they added the topical steroid, betamethasone dipropionate, which is a Class I or II, to try to alleviate the itching from the fungal infection, and they found that the fungal infection actually did clear somewhat quicker.

The problem is the terrible side effects which can happen from the usage of the high-potency topical steroid. The ones we usually see are what are called striae distensae, which are basically stretch marks, and they can last forever. They're extremely unsightly, they are impossible to treat. Sometimes your body clears, though more often they don't.

So in some ways, the usage of Lotrisone, although effective for the tinea or the fungal infection, the treatment was worse than the disease because the patients wound up with striae distensae, so much so that the American Academy of Pedriatics put out an advisory that Lotrisone should not be used in the pediatric age group because of the side effects of the striae distensae.

So at the time I was thinking, myself, that perhaps if we lowered the potency of the cortisone of the steroid cream to a low to a low-medium potency, we would still get efficacy in terms of treating the tinea, or fungal infection, and also we would decrease the itching to a significant degree so the patients would clear just as quickly as with the high-potency steroid.

So what I did is, I took my patients who had significant tinea or fungal infections, and I had them use a standard antifungal, and I had them use a -- and we used alongside with it, in a formulation, a low potency, low to low-medium potency steroid, and we made -- we used several different types of steroids, we used several different types of antifungals. And, surprisingly,

they all worked. They worked beautifully. The patients were thrilled, the itching went way down, inflammation went way down. And the best news, of course, was that there were absolutely no side effects, and I mean zero side effects. There was no striae distensae or stretch marks, there was no hypopigmentation. So I was thrilled with the results, and we continue to use it in my office to this day.

So that was the nature of my invention, that I figured, I hoped counter intuitively, that if we lowered the cortisone, the steroid strength, we would still get the advantages of the higher-potency steroid without the severe side effects, and that's exactly what happened. Thank you.

JUDGE SCHEINER: Thank you.

DR. GOLDSTEIN: Okay. Thank you.

JUDGE SCHEINER: Do you have anything further? Judge Walsh, can you hear me?

JUDGE WALSH: No questions. Thank you.

MR. TERAPANE: Okay.

JUDGE SCHEINER: I'm not used to this.

MR. TERAPANE: No. I understand. It's new for us as well, so --

JUDGE SCHEINER: Do you have anything further?

JUDGE GREEN: No.

MR. TERAPANE: Okay.

JUDGE SCHEINER: Well, thank you for coming in. I think we understand the issue.

MR. TERAPANE: Thank you for your time, we appreciate it.

JUDGE SCHEINER: And thank you for your explanations.

MR. TERAPANE: Okay, thank you.

DR. GOLDSTEIN: Thank you.

MR. TERAPANE: Thank you very much.

DR. GOLDSTEIN: Judge, thank you.

MR. TERAPANE: Have a good day, thank you.

JUDGE SCHEINER: Thank you.

DR. GOLDSTEIN: Thank you.

(Whereupon, the proceedings, at 9:25 a.m., were concluded.)